

		I	II
human EF2K	122	GEWLDDEVLIKMASQ <b>F</b> GRGAMRECFTKKLSNFLHAQ-----QWKGASNYV <b>VAK</b> RYIEPVD	
C. e. EF2K	108	KQWTEIDVDVRLHPDS <b>F</b> ARGAMRECYRLKKCKSHGTSQ-----DW--SSNY <b>VAK</b> RYICQVD	
MHCK A	570	NKWLRLSMKI.KVERKP <b>F</b> AEAGALREAYHTVSLGVGTDENYPFLGTTTKI.FPPIEMISPKNNEAMTQLKNGTK <b>FVL</b> KLYKKEAE	
MHCK B	130	AQWTCATATLVKVEVP <b>V</b> AEAGAFRKAYHTLDLSKSGA-----SGRY <b>VSK</b> IGKK----	
FC-AN09	1	IVCVSIEKTP <b>F</b> AKGSCRTAHKLKDWSQP-----DQGLV <b>GK</b> FSTNKK-	
consensus		**W*****O*O**** <b>F</b> ** <b>G</b> ** <b>R</b> **O*****+***** <b>OV</b> * <b>K</b> *****	

human EF2K	178	-----RDVYFEDVRLQMEAKLWGEENRHHKPPKQVDIMQMCIIELKDR-----PGKPLF-HLEHYIEGKYIKYNSNSGFVRRDNDI	IiI	IV
C. e. EF2K	162	-----RRVLFDDVRLQMDAKLWAEENRYNRPKKIDIVQMCVIEIMDV-----KGSPLY-HLEHFIEGKYIKYNSNSGFVSNAA-		
MHCK A	653	QQASRELYFEDVKMQMVCRDWGNKFNQKKPPKKIEFLMSVWVELIDRSPSSNGQPILCSIEPLLVGEFKNNNSYGAVLTN--		
MHCK B	177	-PTPRPSYFEDVKMQMIAKKWADKYNFKPPKKIEFLQSCVLEFVDRRTSSD---LICGAEPYVEGQYRKYNNSNSGFVSNDE-		
FC-AN09	42	--TTDRDSYFTDVLMQTFCAKWAEKFNKPPKPIITFLPSYVYELIDHPPPY---PV-CGGEPIEGDYKKHNNNSGYVSSDA-		
consensus		****R**QF**DV*QQ*****W*****ON****PPK*O*OO*****E*OO*G*O*K*N*N*G*V*****		

human EF2K	252	RLTPQAFSHTFERSGHQLIVVDIQGVGDLYTDPQIHETGTDFGDNLGVRCMALFFYSHACNRICESMGLAPFDLSPREDD
C. e. EF2K	235	RLTPQAFSHTFERSGHQMMVVDIQGVGDLYTDPQIHVVGTDYGDGNLGRMALFFHSHRCNDICETMDLSNFELSPPELE
MICK A	734	RSTPQAFSHTYELSNKQMIVVDIQGVDDLYTDPQIHPTPDGKGFLGNLKGAGINKFITTHKCNVACALLDL-DVKLG----
MICK B	254	RNTPQSFHFTYEHLSNIQLLIIDIQGVGDHYTDPQIHLYDGVGFGIGNLGQKGFKEFLDTHKCNVICQYI,NLQ3IN-----
FC-AN09	118	RNTPQSFHSFSELSNHELLIVDIQGVNDFYTDPQIHTKSGEGFGEGLNETGFHKFLQTHKCNVPVCDFLKLKPIN-----
consensus		R <sup>4</sup> TPQ <sup>4</sup> FSHF <sup>4</sup> OE <sup>4</sup> S <sup>4</sup> * <sup>4</sup> o <sup>4</sup> o <sup>4</sup> o <sup>4</sup> o <sup>4</sup> DIQGV <sup>4</sup> D <sup>4</sup> o <sup>4</sup> YTDPQIH <sup>4</sup> T <sup>4</sup> G <sup>4</sup> * <sup>4</sup> o <sup>4</sup> G <sup>4</sup> GNLG <sup>4</sup> * <sup>4</sup> Go <sup>4</sup> * <sup>4</sup> FO <sup>4</sup> * <sup>4</sup> H <sup>4</sup> CN <sup>4</sup> * <sup>4</sup> o <sup>4</sup> C <sup>4</sup> * <sup>4</sup> L <sup>4</sup> * <sup>4</sup> o <sup>4</sup> *****

human	EF2K	335	AVNQNTKLLQSAKT--ILRGTEEEKCGS
C. e.	EF2K	318	ATEVAMEVAAKQKSCIVPP <b>T</b> VFEARR
MHCK A		811	----GVLSGNNK <b>K</b> Q--LQQGT <b>M</b> VPDI
MHCK B		330	-----PKSE <b>K</b> SDC---GT <b>V</b> PRPDL
FC-AN09		194	-----QSK <b>K</b> A--LLRG <b>T</b> LPVVQ <b>L</b>
consensus			***** <b>K</b> ***** <b>T</b> *****

# Figure 1A

601-1-098CIP

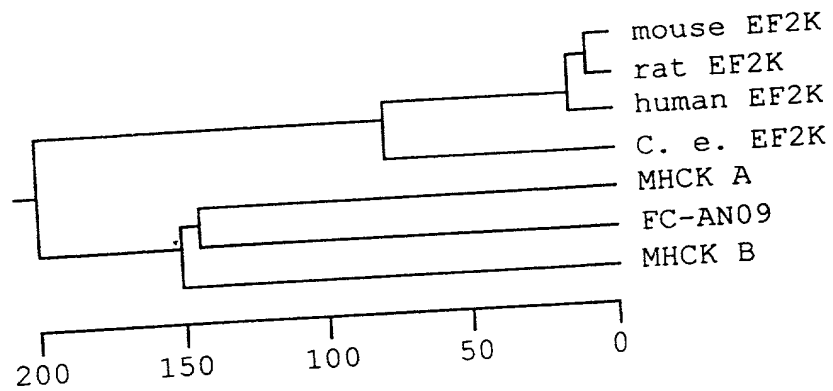


Figure 1B

601-1-098CIP

human eEF-2K	1	.....R.....QSP.....DG.....G.....E.....	44
C. elegans eEF-2K	1	MTIDTTNESDNPTNSPGLEASARTFSLNASKMVR-----ITD	38
mouse eEF-2K	1	MAEDLIFCLEGVGGRCRAGHNADSDTDSDDDEGYFICPTD	44
human eEF-2K	45	.PS.....N...NK.....S.RY.SS.....N.....Q.....	93
C. elegans eEF-2K	39	DYADEVFTEQNDVVIKPRMD-----PLHVRKLMETWRKAARPART	79
mouse eEF-2K	45	DHMSNQNVSSKVQSYSNLTKECGS-TGSPASSFHFKEAWKHAEKAK-	92
human eEF-2K	94	.....R.....D.....	143
C. elegans eEF-2K	80	NYIDPWDEENIHEYPVQRAKRYRYSAIRKQWTEIDVRLHPDSFARGAM	129
mouse eEF-2K	93	HMPDPWAEFHLEDIATEHATRHRYNVVTGEWLKDEVLIKMASQPFGRGAM	142
MHCK A	572	WIRLSMKLKVVERKPPFAEGAL	591
human eEF-2K	144	.....R.....D.....	166
C. elegans eEF-2K	130	RECRLKKCS-----KHGTSQDW--SN	150
mouse eEF-2K	143	RECFFRTKKLS-----NFLHAQQWKGN	165
MHCK A	592	REAYHTVSLGVGTDENYPLGTTTKLFPPIEMISPISKNNNEAMTQLKNGTK	641
human eEF-2K	167	.....D.....R.....E.....	212
C. elegans eEF-2K	151	YVAKRYICQVD-----RRVLEDDVRLQMDAKLWAEFYNRYNPPKKIDIVQM	196
mouse eEF-2K	166	YVAKRYIEPVD-----RSVYFEDVQLQMEAKLWGEDYNRHKPPKQVDIMQM	211
MHCK A	642	EVLKLYKKEAEQQASRELVFEDVKMQMVCRDWGNKFNOKKPPKKIEFLMS	691
human eEF-2K	213	.....K.....	256
C. elegans eEF-2K	197	CVIEMIDVK-----GSP-LYHLEHIEGKYIKYNSNSGFV-S-NAAARLTPO	239
mouse eEF-2K	212	CIIEIKDRP-----GQP-LFHLEHYIEGKYIKYNSNSGFVRDDNI-RLTPQ	255
MHCK A	692	WVVELIDRSPSSNGQPIILCSIEPIILVGEFEKKNNSNYGAVILT-N-RSTPQ	738

Figure 2A

601-1-098CIP

human	eEF-2K	257	.....T.....	306
C.elegans	eEF-2K	240	AFSHFTFERSGHOMVVDIQGVGDLYTDPQIHTVVGTDYGDGNLGTIRGMA	289
mouse	eEF-2K	256	AFSHFTFERSGHQIIVVDIQGVGDLYTDPQIHTTEKGTDFGDNLGVRGMA	305
MHCK A		739	AFSHFTYELSNKQMIVVDIQGVDDLYTDPQIHTPDCKGFGIGNLKGACIN	788
human	eEF-2K	307	.....E.....A.....R.....N.K.....	354
C.elegans	eEF-2K	290	LEFHSHRCNDICEFMDLSNFEFLSPPEIEATEVAMEVAAKQKKSCIVPPTV	339
mouse	eEF-2K	306	LEFFYSHACNRICQSMGLTFDLSPREQDAVNQSTRLLQSAKT--ILRGTE	353
MHCK A		789	KFITTHKCNVCAVLDL	805
human	eEF-2K	355	.....V...G...---RP.....	400
C.elegans	eEF-2K	340	FEARNRISSECVHVEHGISMDDQLRKRKTL--NQSSDLSAKSHNEDCV	386
mouse	eEF-2K	354	EKCGSPRIRTLSS--RPPLL-LRLSENSGDENMSDVTFDSLPSSPSSA	399
human	eEF-2K	401	.....S.....AS.....HL.....E.....G	449
C.elegans	eEF-2K	387	CPECIPVVEQLCEPCSEDEDEEEDYPRSEKSGNSQKSRMSISSTRSS	436
mouse	eEF-2K	400	TPHSQKLDH-LHWPVFGDLDNMGPRDHRMDNHRDSENSGDSGYPSSEKRS	448
human	eEF-2K	450	-E.....--YS...-KY.....K.....S....	494
C.elegans	eEF-2K	437	GDESASRPKCGFVDLNSLRQRHDSFRSSVCTYSMNSSRQTRDTEKDEFW	486
mouse	eEF-2K	449	-DLDDPEPREHG--HSNGNR-RHESDEDSLGS-SGRVCVETWNLNPSRL	493
human	eEF-2K	495	.....A.....E.K.....I.....	532
C.elegans	eEF-2K	487	KVLRKQSVPANILSLQLOQMAANLENDEDVPQVTGHQFVSLGQTHIDLSR	536
mouse	eEF-2K	494	HLPRPSAVALERQRLNALDLGRKIGK-----SVLGKVHLAMVR	531

Figure 2B

601-1-098CIP

human eEF-2K	533	.....G.....Q.....V.....N.....	565
C.elegans eEF-2K	537	YHELGREVEVDSEHKEMLEGSENDARVPIKYDKSAIFHLDIARKCIGLE	586
mouse eEF-2K	532	YHEGGRFCEKDEE-----WDRESAIFHLEHAADLGELE	564
human eEF-2K	566	.....	596
C.elegans eEF-2K	587	AVLTSAHIVLGLPHELLKEVTVDLFPNGFGEQENGIRADKGQKPCDLEE	636
mouse eEF-2K	565	AIIVGLGIMYSQLPHEILLADVSLKE-----TENKTK-----	595
human eEF-2K	597	.....Q.....S.Q.....L.....	645
C.elegans eEF-2K	637	FGSDILMEIAAEAGDKGAMLYMAHAAYETGQHILGNRRTDYKKSIDWYQRVV	686
mouse eEF-2K	596	-GFDYLLKAAEAGDRHSMILLVARAFDTGLNLSFDRCDWSEALHWYNAL	644
human eEF-2K	646	-----M.....M.....R.MM.....F...Y..E.D....	689
C.elegans eEF-2K	687	GFQEEELDSDCCKTTFSFAPLTRHEILAKMAEMYKEGGYGLNQDFERA	736
mouse eEF-2K	645	-----ETTDCEG-GEYDGIQDEPQYALLAREAEMLLTGGFGLDKNPQRS	688
human eEF-2K	690	.....Q.....	725
C.elegans eEF-2K	737	YGLFNEAAAEAAEAMNCKLANKYYEKAEMC-----GE	768
mouse eEF-2K	689	GDLYTQAAAEAAEAMKGRLANQYYEKAEEAWAQMEE	724

Figure 2C

601-1-098CIP

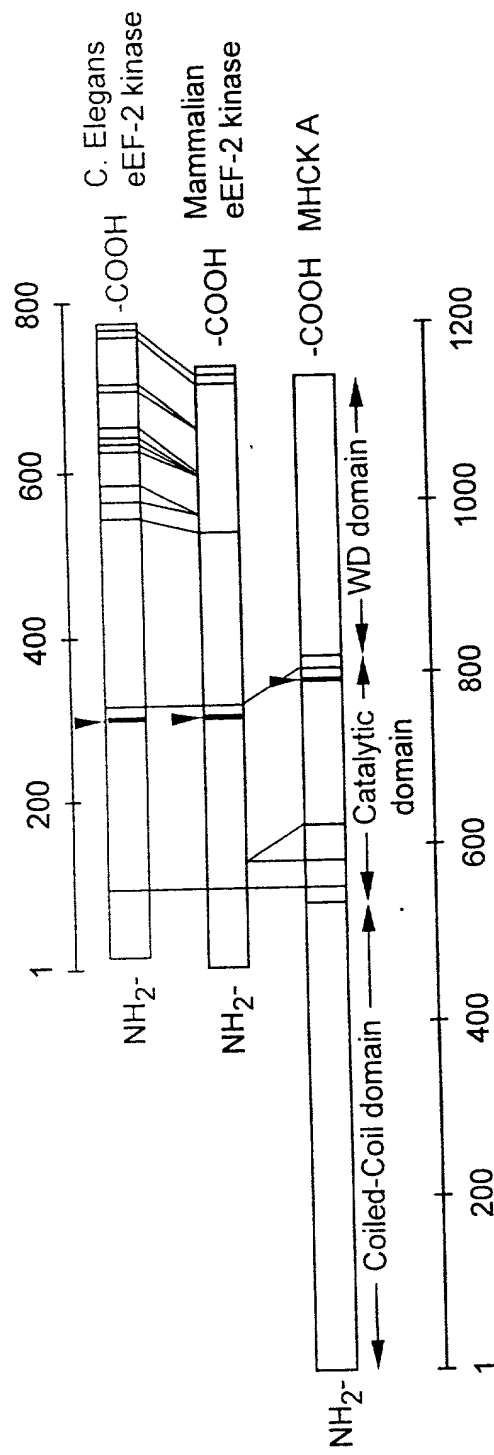


Figure 3

## Current Biology

## Figure 4

1 cgggcgcggg cgcgccctc tggccagtea cccggcggag ctgggtcgac aattatgaaa  
 61 gactcgactt ctgctgctag cgctggagct gagttagttc tgagaagggt tcccggggct  
 121 gtccttggtt ggtggcccggt gccacgcgct cgggagacgc ttccgtagat gtggctgcag  
 181 gccgcggagg tggaggagga gccgctgccc ttccggagtc cgccccgtga ggagaatgtc  
 241 ccagaaatcc tggatagaga gcactttgac caagagggag tgtgtatata ttataccaag  
 301 ctccaaagac cctcacagat gtcttccagg atgtcagatt tgtcagcaac ttgtcagatg  
 361 tttctgtggt cgtttgggtc agcaacatgc atgtcttact gcaagtcttg ccatgaaata  
 421 ctcagatgtg agattgggtg aacactttaa ccaggcaata gaagaatggt ctgtggaaaa  
 481 gcacacggag cagagcccaa cagatgctta tggagtcac c aattttcaag ggggttctca  
 541 ttctacaga gctaagtatg tgagactatc atatgatacc aaacctgaaa tcattctgca  
 601 acttctgctt aaagaatggc aaatggagtt acccaaactt gttattttctg tacatggagg  
 661 catgcagaag tttgaacttc atccaagaat caagcagttg cttggaaagg gtcttattaa  
 721 agctgcagtt acaaccggag cttggatttt aactggagga gtcaatacag gtgtggcaaa  
 781 acatgttggg gatgccctca aagaacatgc tccagatca tctcgaaaaa ttgactat  
 841 tggaaatgct ccatggggag tgatagaaaa cagaaatgat cttgttggga gagatgtggg  
 901 tgctccttat caaaccttat tgaatccctt gagcaaattg aatgttctga ataacttaca  
 961 ctcccatttc atcttgggtg atgatggcac tgttggaaag tatggggcag aagtcagact  
 1021 gagaagagaa cttgaaaaaa ccattaatca gcaaagaatt catgctagaa ttgggcaagg  
 1081 agttcctgtg gtggctttga tatttgaagg cgggccaaat gtcactctta cagtactgga  
 1141 gtacctcag gaaagcccc cagttccagt tgttgtgtgt gaaggacag gcagagctgc  
 1201 agatttacta gcctatctcc acaaacagac agaggaagga ggaaatcttc ctgatgcagc  
 1261 agagcctgat attatatcaa ctatcaagaa aacatttaac tttggccaga gtgaagcagt  
 1321 tcattttattt caaacaatga tggagtgtat gaaaaaaaaa gagcttatca ctgtttttca  
 1381 cattggatca gaggatcatc aagatataga tgtggccata ctcactgcac tgtgaaagg  
 1441 tactaatgca tctgcatttg accagcttat cttacactg gcattgggaca gattgatat  
 1501 tgccaaaaat catgtatttg tttatggaca acagtggctg gttggatcct tggaaacagg  
 1561 tatgtctgat gctcttgtaa tggacagagt ttcatttcta aaacttctta ttgaaacagg  
 1621 agtaagcatg cataaattcc ttaccattcc cagactggaa gaactttata acactaaaca  
 1681 aggtccaacc aatccaatgt tgttccatct cattcgggat gtcaagcagg gtaatctccc  
 1741 cccggggtac aagatcactt taattgatat aggacttgtg attgagtatc tcattggagg  
 1801 aacctacaga tgcacatata cagcaaaacg ttttcgattg atatataata gtcttgggtg  
 1861 aaataaccgg aggtcaggtc gaaatacctc cagcagcacc cctcagttgc gaaagagtca  
 1921 tgaaactttt ggcaatagag ctgataaaaa ggaaaaaatg agacacaatc atttcattaa  
 1981 aacagcccaa ccctacagac caaagatgga tgcactatg gaagaaggaa agaagaaaag  
 2041 aaccaagat gaaattgtag atatagatga tccagagacc aagcgcttct ctatcctct  
 2101 taatgaatta ttaatttggg cttgccttat gaagaggcag gtcattggccc gctttttatg  
 2161 gcagcatggt gaagaatcaa tggctaaagc attagttgcc tgtaaaatct atcgttcaat  
 2221 ggcttatgat gcaaagcaga gtgacctggt agatgatact tcagaggaac tgaagcagta  
 2281 ttccaatgat tttggccaac tggcagttga attactggaa cagtccttca gacaggatga  
 2341 aacgatggct atgaaattac tcacttatga actcaaaaac tggagtaatt caacctgcct  
 2401 caagttagca gtttcttcaa gacttagacc tttttagct cactctgtta cacagatgtt  
 2461 gttatctgat atgtggatgg gacggctgaa tatgagaaaa aattcctggt ataaggatc  
 2521 attaaagcatt ttagttccac ctgccatatt aatgctagag tataaaacca aggctgaaat  
 2581 gtccatatac ccacaatctc aagatgctca tcaaatgacg atggaggata gtgaaaacaa  
 2641 ttttcacaac ataacagaag agatacccat ggaagtattt aaagaagtaa agattttgga  
 2701 cagcagtgat ggaaagaatg aaatggagat acatattaaa tcaaaaaagc ttccaatcac  
 2761 acgaaaattt tatgcctttt atcatgcacc aattgtaaaag ttctggttta acacattggc  
 2821 atatttagga tttctgatgc tttatcatt tgtagttctt gtaaaaatgg aacagttacc  
 2881 ttcagttaaa gaatggattg ttatcgctta tttttttacc tatgctattg aaaaagtcgg

Figure 5A



2941 tgagggtcttc atgtctgaag ctgggaaaat cagccagaag attaaagtat gggttagtga  
 3001 ctacttcaat gtcagtgaca caattgccat cattctcttc tttgttggt ttggactaag  
 3061 atttggagca aaatggaact atattaatgc atatgataat catgtttttg tggctggaag  
 3121 attaatattac tgtcttaata taatattttg gtatgtgctg ttgctagact ttctagccgt  
 3181 aaatcaacag gcaggacctt atgtaatgat gattggaaaa atgggtggcca atatgttcta  
 3241 cattgtagtg ataatggctc ttgtattgct tagttttggt gttcccagaa aagcaatact  
 3301 ttatccacat gaagaacat cttggctctc tgctaaagat atagttttct atccactctg  
 3361 gatgattttt ggtgaagttt atgcatatga aattgatgtg tgtgcaaatg actccactct  
 3421 ccogacaatc tgtggctctg gaacttggtt gactccattt cttcaagcag tctacctctt  
 3481 tgtacagtat atcattatgg ttaatctcct tatcgcattt ttcaataatg tatatttaca  
 3541 agtgaaggca atttccaata ttgtatggaa gtatcagcgg tatcatttta ttatggctta  
 3601 tcatgaaaaa ccagtcctgc ctccctctct tatcatctc agccatatag ttctactggt  
 3661 ttgctgtgta tgcaaaagaa gaaagaaaga taagacttcc gatgggcca aacttttctt  
 3721 aacagaagaa gatcaaaaga aactccatga ttttgaagag cagtgtgttg agatgtactt  
 3781 tgatgagaaa gatgacaaat tcaattctgg gagtgaagag agaatccggg tcaactttga  
 3841 aagagtggag cagatgagca ttcagattaa agaagttgga gatcgtgtca actacataaa  
 3901 aagatcatta cagtctttag attctcaaat tggctcatct caagatctct cagccctaac  
 3961 agtagatata ttgaaaacac ttacagccca gaaagcttca gaagctagta aagtgcacaa  
 4021 tgagatcaca cgagaattga gtatttccaa acacttggct cagaatctta ttgatgatgt  
 4081 tcctgtaaga cctttgtgga agaaacctag tgctgtaaac acactgagtt cctctcttcc  
 4141 tcaaggtgat cgggaaagta ataactcttt tctttgtaat atttttatga aagatgaaaa  
 4201 agacccccaa tataatctgt ttggacaaga tttgccctg ataccccaga gaaaagaatt  
 4261 caacattcca gaggtctggtt cctcctgtgg tgccttatte ccaagtgtct tttctcccc  
 4321 agaattacga cagagacgac atggggtaga aatgttaaaa atatttaata aaaatcaaaa  
 4381 attaggcagt tcacctaata gttcaccaca tatgtcctcc ccaccaacca aattttctgt  
 4441 gagtacccca tcccagccaa gttgcaaaag ccacttgga tccacaacca aagatcaaga  
 4501 acccattttc tataaagctg cagaagggga taacatagaa tttggagcat ttgtgggaca  
 4561 cagagatagt atggacttac agaggtttaa agaaacatca aacaaaataa gagaactggt  
 4621 atctaattgat actcctgaaa acactctgaa acatgtgggt gctgctggat atagtgaatg  
 4681 ttgtaagact tctacttctc ttcactcagt gcaagcagaa agctgtagta gaagagcgtc  
 4741 gacggaagac tctccagaag tcgattctaa agcagctttg ttaccggatt gggtacgaga  
 4801 tagaccatca aacagagaaa tgccatctga aggaggaaca ttaaattggtc ttgcttctcc  
 4861 atttaagccc gttttggata caaattacta ttattcagct gtggaaagaa ataacctgat  
 4921 gaggttgtca cagagtattc ccttcgttcc tgtacctcca cgaggcgagc ctgtcacagt  
 4981 gtaccgtctg gaggagagtt ctcccagtat actgaataac agcatgtctt catggtctca  
 5041 gctaggcctc tgtgcaaaaa ttgagttttt aagtaaagag gaaatgggag gtggtttacg  
 5101 aagagcagtc aaagtgtgtg gtacctgggt agagcacgat atcctgaagt cagggcatct  
 5161 ctatatcatt aagtcatttc ttctgaggt gataaacaca tgggtcaagca tttataaaga  
 5221 agatacgggt ctacatctct gtctcagaga aatacaacaa cagagagcag caaaaagct  
 5281 cacatttgcc tttaatcaga tgaaacccaa atccatacca tattctccaa gggtccttga  
 5341 agtttttctg ttgtactgcc attcagcagg gcagtgggtt gctgtagaag agtgcagac  
 5401 tgggtgaattt agaaaataca acaacaataa tgggtgatga atcattccta caaatactct  
 5461 agaagagatc atgctagcct ttagccactg gacctatgaa tataccagag gggagttact  
 5521 ggtacttgac ttacaaggag tgggagaaaa cttgactgac ccactctgta taaaagctga  
 5581 agaaaaaaga tctgtgaca tgggttttgg ccttgccaat ctaggagaag atgcaataaa  
 5641 aaacttcaga gccaaacatc actgtaatte ttgtgtcga aagcttaaac ttccagattt  
 5701 gaagaggaat gactacacgc ctgataaaat tatatttctc caggatgagt catcagattt  
 5761 gaatcttcaa tctggaaatt ccaccaaaga atcagaagca acaaattctg ttcgtctgat  
 5821 gttatagtgc tgagtcattg gtttttgcct acacttcaca aaagtgtaac tgtcagtttt

Figure 5B

5881 cctttcgggg gaattgatga tataggaaga tgtgtgcaaa atgagcttgc tggccccaca  
5941 catagtctag aggtaatggt ctcatgtaaa aacgcctgga ggctgcagat gacagctgga  
6001 aagtgcctagc tggcagagag tcagtgtctc cggctggtga agggcgggaa ccttgctgct  
6061 gagagtgggtg gttctctcac ctggtgcagg accattaacc aaagtcaagt cttcagattt  
6121 gattggctgc tcagtcacag ccattcagct aaggaaacta aattgcgcag ctttttaaat  
6181 ggctgaagtc ttctcagtt tgtgtcttat gataatgatg ttagctctca actaggtggt  
6241 tgtggccacg ggagaactac tccttacaat tttgcttcac aggcattgta caaagcctgc  
6301 actgaaaacc gtttgtcttc cctctctccc tccctctttt ccctgtagta ttgaggatca  
6361 aaccaggggc ctcatagaaga ccattttcta agagacattt tatttaagaa tcaactatag  
6421 agtctatggt tatggataca gccagttttt gttaacaaa acctgaattg tgcaaaaggg  
6481 ttttttaaca tttatcaatg ttaagtaaaa gaaagccatg ataaataaga attaactcac  
6541 tgttcaatgg gtgtttcctg tgaggaaggt tacagttgta acagcctgca gttgcataca  
6601 tctccaaaaga tttacagact tagtgtatca aatcagagtg tcatgtgagc tctcacattg  
6661 aaaattctat aggaatgtgt caatgtgaat tctatttctg gtacttaaga aatcagttgt  
6721 tggattatcc ttatacagta tagggagatc acaatacaac tttatgccaa taaaatctaa  
6781 ctttaattgcc cagatatattt tgcataattt gcaacaagaa aagcttatca tttgactcaa  
6841 gttttatgct ttctctttct tttcatttcc taggtactaa ttttaatttt tatttggaag  
6901 gagcagtgta aagcttactt gtattcaata gtgtatctca tagatacaga caaggcgcga  
6961 gagataagct gttaaatagt gtttaatggt gatgtggaga gaaaggtgta ttacttaaaa  
7021 atactatacc atatacgttt tgtatatcat taaatcttta aaagaaatta aatttattct  
7081 tgtttacaaa

Figure 5C

MSQKSWIESTLTKRECVYIIPSSKDPHRCCLPGCQICQQLVRCFCGRLVKQHACFTASLAM  
KYSDVRLGEHFNQAIEEWSVEKHTEQSPTDAYGVINFQGGSHSYRAKYVRLSYDTKPEII  
LQLLLKEWQMELPKLVISVHGGMQKFELHPRIKQLLGKGLIKAAVTTGAWILTGGVNTGV  
AKHVGDALKEHASRSSRKICTIGIAPWGVNIENRNDLVGRDVVAPYQTLNPLSKLNVLNN  
LHSHFILVDDGTVGKYGAEVRLRRELEKTINQQRIHARIGQGVVVALIFEGGPNVILTV  
LEYLQESPPVPVVVCEGTGRAADLLAYIHKQTEEGGNLPDAAEPDIIISTIKKTFNFGQSE  
AVHLFQTMMECMKKELITVFHIGSEDHQDIDVAILTALLKGTNASAFDQLILTAWDRV  
DIAKNHVFVYGQQWLVGSLAQMLDALVMDRVSFVKLLIENGVSMMHKFLTIPRLEELYNT  
KQGPTNPMLFHLIRDVKQGNLPPGYKITLIDIGLVIEYLMGGTYRCTYTRKRFRILIYNSL  
GGNNRRSGRNTSSSTPQLRKSHETFGNRADKKEKMRHNHFIKTAQPYRPKMDASMEEGKK  
KRTKDEIVDIDDPETKRFPPYPLNELLIWACLMMKRQVMARFLWQHGEESMAKALVACKIYR  
SMAYEAKQSDLVDDTSEELKQYSNDFGQLAVELLEQSFRQDETAMKLLTYELKNWSNST  
CLKLAVSSRLRPFVAHTCTQMLLSDMMWGRNLNMRKNSWYKVIILSILVPPAILMLEYKTKA  
EMSHIPQSQDAHQMTMEDSENNFHNITEEIPMEVFKEVKILDSSDGKNEMEIHISKKLP  
ITRKFYAFYHAPIVKFWFNTLAYLGFLMLYTFVVLVKMEQLPSVQEWIVIAIYIFTYAIEK  
VREVFMSSEAGKISQKIKVWFSDYFNVSDTIAIISFFVGFLRFGAKWNYINAYDNHVFVA  
GRLIYCLNIIFWYVRLDFLAVNQAGPYVMMIGKMVANMFYIVVIMALVLLSFGVPRKA  
ILYPHEEPSWSLAKDIVFHPYWMIFGEVYAYEIDVCANDSTLPTICGPGTWLTPFLQAVY  
LFVQYIIMVNLLIAFFNNVYLQVKASINIVWKYQRYHFIMAYHEKPVLPPLIILSHIVS  
LFCCVCKRRKKDKTSDGPKLFLTEEDQKKLHDFEEQCVEMYFDEKDDKFNSGSEERIRVT  
FERVEQMSIQIKEVGDRVNYIKRSLQSLDSQIGHLQDLSALTVDTLKTLTAQKASEASKV  
HNEITRELSISKHLAQNLIDDVVRPLWKKPSAVNTLSSSLPQGDRESNNPFLCNIFMKD

Figure 6A

EKDPQYNLFGQDLFVIPQRKEFNIPEAGSSCGALFPSAVSPPELRQRRHGVEMLKIFNKN  
QKLGSSPNSSPHMSSPPTKFSVSTPSQPSCKSHLESTTKDQEPIFYKAAEGDNIEFGAFV  
GHRDSMDLQRFKETS NKIRELLSNDTPENTLKHVGAAGYSECCKTSTSLHSVQAESCRR  
ASTEDSPEVDSKAALLPDWLRDRPSNREMPSEGGTLNGLASPFKPVLDTNYYYYSAVERN  
LMRLSQSIPFVPVPPRGEFVTYRLEESSPSILNNSMSSWSQLGLCAKIEFLSKEEMGGG  
LRRAVKVLCTWSEHDILKSGHLYI IKSFLPEVINTWSSIYKEDTVLHLCLEIQQQRAAQ  
KLTFAFNQMKPKSIPYSPRFLEVFLLYCHSAGQWFAVEECMTGEFRKYNNNNGDEI IPTN  
TLEEIMLAFSHWTY EYTRGELLVLDLQGVGENLTDPSVIKAEKRS CDMVFGPANLGEDA  
IKNFRAKHHCNSCCRKLKLPDLKRNDYTPDKIIFPQDESSDLNLQSGNSTKESEATNSVR  
LML

Figure 6B

**Figure 7A**

MSQKSWIESTLTKRECVYIIPSSKDPHRCLPGCQICQQLVRCFCGRLVKQHACFTA  
SLAMKYSDVKLGDHFNQAIEEWSVEKHTEQSPTDAYGVINFQGGSHSYRAKYVRL  
SYDTKPEVILQLLLKEWQMELPKLVISVHGGMQKFELHPRIKQLLGKGLIKA AVT  
TGAWILTGGVNTGVAKHVG DALKEHASRSSRKICTIGIAPWGV IENRNDLVGRD VV  
APYQ TLLNPLSKLNV LNNLHSHFILVDDGT V GKYGAEVRLRRELEKTINQQRIHAR  
IGQGV PVVALIFEGGPNVILT VLEYLQESPPVPVVVCEGTGRAADLLAYIHKQTEEG  
GNLPDAAEPDIISTIKKT FNFGQNEALHLFQTLMECMKRKELITVFHIGSDEHQDID  
VAILTALLKGTNASAFDQLILTLAWDRVDIAKNHVFVYGGQQLVGSLEQAMLDAL  
VMDRVA FVKLLIENGVS MHKFLTIPRLEELYN TKQGPTNPMLFHLVRDV KQGNLP  
PGYKITLIDIGLVIEYLMGGTYRCTYTRKRFR LIYNSLGGNNRRSGRNTSSSTPQLR  
KSHE SFGNRADKKEKMRHNHFIKTAQPYR PKIDTVMEEGKKKRTKDEIVDIDDPE  
TKRFPYPLNELLIWACL MKRQVMARFLWQHGEESMAKALVACKIYRSMAYEAKQ  
SDLVDDTSEELKQYSNDFGQLAVELLEQSFRQDET MAMKLLTYELKNWSNSTCLK  
LAVAAKHRDFIAHTCSQMLLTDMWMGRLRMRKNPGLKVLSILVPPAILLLEYKT  
KAEMSHIPQSQDAHQMTMDDSEN NFQ NITEEIPMEVFKEVRILDSNEGKNEMEIQM  
KSKKL PITRKFYAFYHAPIVKFWFNTLAYLGFLMLYTFVVLVQMEQLPSVQEWIVI  
AYIFTYAIEKVREIFMSEAGKVNQKIKVWFSDYFNISDTIAHSFFIGFGLRFGAKWNF  
ANAYDNHVFVAGRLIYCLNIIFWYVRLLD FLAVNQQAGPYVMMIGKMVANMFYIV  
VIMALVLLSFGVPRKAILYPHEAPSWTLAKDIVFHPYWMIFGEVYAYEIDVCANDS  
VIPQICGPGTWLTPFLQAVYLFVQYIIMVNLLIAFFNNVYLQVK AISNIVWKYQRYH  
FIMAYHEKPVLPPLIILSHIVSLFCCICKRRKKDKTSDGPKLFLTEEDQKKLHDFEE  
QCVEMYFNEKDDKFHSGSEERIRVTFERVEQMCIQIKEVGDRVNYIKRSLQSLDSQI  
GHLQDLSALTVDTLKTLTAQKASEASKVHNEITRELSISKHLAQNLIDDGPVRPSV  
WKKHGVVNTLSSSLPQGDLESNNPFHCNILMKDDKDPQCNIFGQDLPVPQRKEF  
NFPEAGSSSGALFPSAVSPPELRQRLHGVELLKIENKNQKLGSSTSI PHLSSPPTKFF  
VSTPSQPCKSHLETGTKDQETVCSKATEGDNTEFGAFVGHRDSMDLQRFKETS N  
KIKILSNNNTSENTLKR VSSLAGFTDCHRTSIPVH SKQEKISRRPSTEDTHEVDSKAA  
LIPVWLQDRPSNREMPSEEGTLNGLTSPFKPAMDTNYYYSAVERN NLMRLSQSIPF  
TPVPPRGEPVTVYRLEESSPNILNNSMSSWSQLGLCAKIEFLSKEEMGGGLRRAVK  
VQCTWSEHDILKSGHLYIHSFLPEVVNTWSSYKEDTVLHLCLEIQQRAAQKLT  
FAFNQMKPKSIPYSPRFLEVFLLYCHSAGQWFAVEECMTGEF  
RKYN NNNNGDEIPTNTLEEIMLAFSHWTYEYTRGELLVLDLQGVGENLTDPSVIKA  
EEKRSCDMVFGPANLGEDA IKNFRAKHHCNSCCRKLKLPDLKRNDYTPDKIIFPQD  
EPSDLNLQPGNSTKESESTNSVRLML

Figure 7B

## Figure 8A

T03T0T 2622660

601-1-098CIP

ESAEPLTQSDKRETSHTTAAATGRSSHADARECAISTQAEQEAQTLQTSTDSVSKEGNTNCKGEGMQVN  
 TLFETSQVPDWSDPPQVQVQETVRETISCSQMPAFSEPAAGEESPFTGTTTISFNLGGVHKENASLAQHSEV  
 KPCTCGPQEEKQDRDNIPDNFREDLKYEQSISEANDETMSPGVFSRHLPKDARADREFVAVSVASPEP  
 TDTALTLENVCDEPRDREAVCAMECFEASDQGTCTDIDSLVGTVPVDNYSQPEICSVDTTELAEQNKVSD  
 LCSSNDKLTLEVFQTVQVSETSVSTCKSSKDGNSVMSPLFISTFTLNISHTASEGATGENLAKVEKSTYPLAS  
 TVHAGQEQSPSNSGGLDETQLLSENPNLVQFKEGGDKSPSPAADTTATPASYSSIVSFPWEKPTTLTAN  
 NECFQATRETVTIATEVHPAKYLAVSIPEDKHAGGTEERFPRASHEKVSQFPSQVQVDHILSGATIKSTKEL  
 LCRAPSVPGVPHHVLQLPEGEGFCSNPLQVDNLSGDKSQTVDRADFRSYEENFQERGETKQGVQQQSL  
 SQQGLSAPDFQQSLPTTSAAQEERNLVPTAPSPASSREGAGQORSGWGTTRVSVVAETAGEEDSQALSNVPS  
 LSDILLESKEYRPGNWEAGNKLKIITLEASA SEIWPPRQLTNSEKASDGGLIIPDKVWAVPDSLKADAVV  
 PELAPSEIALAHSPEDAESALADSRESHKGEEPTISVHWRSLSSRGFSQPRLLESSVDPVDEKELSVTDSLS  
 AASETGGKENVNVNSQDQEEKQLKMDHTAFFKKFLTCPKILESSVDPIDEISVIEYTRAGKPESETTPQGA  
 REGGQNDGNMGHEAEIQSAILQVPCQLQGTILSENRISSQEGSMKQEAQIQPEEAKTAIWQVLPSEGG  
 ERIPSGCSIGQIQESSDGLGEAEQSKKDKAELISPTSLSSCLPIMTHSSLGVDTHNSTGQIHDVPENDIVEP  
 RKRQYVFPVSQKRGTIENERGKPLPSSPDLTRFPCTSSPEGNVTDFLISHKMEEPKEIQLIGETKPPSSSSSS  
 AKTLAFISGERELEKAPKLLQDPCQKGTLCGAKKSREREKSLERAGKSPGTLTAVTGSEEVKRKPEAPGS  
 GHLAEGVKKKILSRVAALRLKLEKENIRKNSAFLKMPKLETSLSHTEEKQDPKPKSCCKREGRAVLLK  
 KIQAEMFPEHSGNVKLSQFAEIHEDSTICWTKDSKSIAQVQRSAGDNSTVSFAIVQASPKDQGLYYCCIK  
 NSYGKVTAEFNLTAEVKQLSSRQDTKGCEEIEFSQLIFKEDFLHDSYFGGRLRGQIAATELHFGEVHRK  
 AFRSTVMHGLMPVFKPGHACVLKVHNAIAYGTRNNDELIQRYKLAQECYVQNTARYYAKIYAAEAQ  
 PLEGFGEVPEIPIFLIHRPENNIPYATVEEELIGEFVKYSIRDGKEINFLRESEAGQKCTFQHWVYQKTS  
 CLLVTDMMQVGMKLTVDVGIATLAKGYKGFGKGNCSMTFIDQFKALHQC�KYCKMLGLKSLQNNNQKQK  
 QPSIGKSKVQTNMSMTVKKAGPETPGEKKT

Figure 8B



1 atgtcccaga aatctctggat taaaggagta ttgacaaga gagaatgtag cacaatcata  
 61 cccagctcaa aaaatcctca cagatgtact ccagtatgcc aagctgcca gaatttaate  
 121 aggtgttact gtggccgact gattggagac catgtctgga tagattatce ctggaccate  
 181 tcagctgcca agggtaaaga aagtgaacaa tggctctgtg aaaagcacac aacgaaaage  
 241 ccaacagata ctttggcac gattaatttc caagatggag agcacacca tcatgccaag  
 301 tatattagaa ctcttatga tacaanaactg gatcatctgt tacatttaac gttgaagag  
 361 tggaaaatgg aactgcccac gcttgtgac tcagtcacatg ggggcatcca gaactttact  
 421 atgcccctca aatttaaaga gatttcagc caaggttgg ttaaagctgc agagacaaca  
 481 ggagcgtgga taataactga aggcataat acagtgtcca agcatgttgg gcatgcttg  
 541 aaateccatt cctctcattc ctgagaaaa atctggacag ttggaatccc tcttggggt  
 601 gtcatgaga accagagaga ccttattgga aaagatgtgg tgtgctgta ccagactctg  
 661 gataaccccc tcagcaagct cacaacactc aacagcatgc actcgcaatt cactctgtct  
 721 gatgatgga cctgtgggcaa gtatggaaat gaaatgaagc tcagaaggaa cctggagaag  
 781 tactctctc tgcagaaaat acactgcgc tcaagacaag gcgtgccggt cgtgggctg  
 841 gtggggaag gcggtcccaa cgtcactctg tcagtgtggg agactgtcaa ggacaaggac  
 901 ccagtgttgg tgtgtgaggg cacaggtagg gcggtgacc tcttggcctt cacacacaaa  
 961 cacttggcag atgaagggat gctgcgacct cagggtgaag aggagatcat ctgcatgatt  
 1021 cagaacactt tcaactttag tcttaaacag tccaagcacc ttctccaaat tctaattggag  
 1081 tgtatgttgc acagggtatg tattaccata ttgatgtctg actctgaaga gcagcaagac  
 1141 ctggacttag caatcctaac agctttgctg aagggcacaa atttatcagc gtcagagcaa  
 1201 ttaaacttgg caatggcttg ggacagggtg gacattgcca agaaacatat cctaatttat  
 1261 gaacaacact ggaagcctga tgccttgga caagcaatgt cagatgcttt agtgatggat  
 1321 cgggtggatt ttgtgaagct ctaaatagaa tatggagtga acctccatcg ctttcttacc  
 1381 atccctcgac tggagagct ctacaataca aaacaaggac ctactaatac actcttgcac  
 1441 catctctgac aagatgtgaa acagcatacc ctcttctcag gctaccgaat aaccttgatt  
 1501 gacattggat tagtagtaga atacctcatt ggtagagcat atcgagcaa ctacactaga  
 1561 aaacatttca gagecctcta caacaacctc tacagaaaat acaagcacca gagacactcc  
 1621 tcaggaaata gaaatgagtc tgcagaaagt acgtgcact cccagttcat tagaactgca  
 1681 cagccataca aattcaagga aaagtctata gtcttcata aatcaaggaa gaagtcaaaa  
 1741 gaacaaaatg tatcagatga cctgagctc actggttctc ttaccctta caatgaactg  
 1801 ctggttggg ctgtgctgat gaaaaggcag aagatggcta tgttctctg gcagcatgga  
 1861 gaggaaggcca cggitaaage cgtgattgag tgtatctct accgggcaat ggcccatgaa  
 1921 gtaaggaga gtcacatggt ggatgatgcc tcagaagagt tgaagaatta ctcaaaacag  
 1981 ttggccagc tggctctgga ctgttggag aaggcattca agcagaatga gcgcatggcc  
 2041 atgacgctgt tgacgtatga actcaggaac tggagcaatt cgacctgect taaactggcc  
 2101 gtgtcgggag gattacgacc ctttgttca catacttga ccagatgct actgacagac  
 2161 atgtggatgg ggaggctgaa aatgaggaaa aactcttgg taaagattat tataagcatt  
 2221 atttaccac ccaccatttt gacactggaa tttaaaagca aagctgagat gtcacatgtt  
 2281 cccagtcce aggaacttca atttatgttg tattacagt accagaacgc cagcagttcc  
 2341 aaagaaagt ctctgtgaa agagtatgat ttggaagggg gccatgatga gaaactggat  
 2401 gaaaatcage attttgttt ggaaagtggg caccaacacc ttccgtggac caggaaagtc  
 2461 tatgagttct acagtgtcc aattgtcaag ttgtgttt atacgatggc gtatttggca  
 2521 ttctcatgc ttttcaacta caccgtgttg gtggagatgc ageccagacc cagcgtgcag  
 2581 gattgtgctg ttacatcta catcttcacc aatgctattg aggtgttcag ggaggtgagt  
 2641 attcagaac ctgggaagt tacccaaaag gtgaaggat ggattagtga gtaactggaac  
 2701 ttaacagaaa ctgtggccat tggcctgttt tcagctggct tegtctctg atggggtgac  
 2761 cctcttttc acacagcggg aagactgate taactcatag acatcataat ctggttctca  
 2821 cggctctctg actctttgc tgtgaatcaa catgcaggtc catatgtgac catgattgca  
 2881 aaaatgacag caaacatgtt ctatattgtg atcatcatgg ccatagctct gctgagcttt  
 2941 ggagtggcag gcaaggccat ccttgcgca aaagagccac catcttggag tctagctega  
 3001 gatattgtat ttgagccata ctggatgata tacggagaag tctatgtgg agaaatagat  
 3061 gttgttcaaa gccagccatc ctgcccctct ggttcttttc ttaactcatt ctgcaagct  
 3121 gtctacctct tctgtcaata tatcatcatg gtgaacctgt tgattgttt ctcaacaac  
 3181 gtttacttag atatggaatc catttcaaat aacctgtgga aatacaaccg ctatcgetac

Figure 9A

3241 atcatgacct accacagaaa gccctggctg ccccccctc tcactctgct gagccacgtg  
 3301 ggccctctcc tcgcgcgcct gtgctgtcat cgagctctc acgaccaaga agagggtgac  
 3361 gttggattaa aactctacct cagtaaggag gatctgaaaa aactctatga ttttgaggag  
 3421 cagtgcgtgg aaaaataact ceatgagaag atggaagatg tgaattgtag ttgtgaggaa  
 3481 cgaatccgag tgacatcaga aagggttaca gagatgtact tcagctgaa agaaatgaat  
 3541 gaaaagggtg cttttataaa ggactctta ctgtctttgg acagccaggt gggacacctg  
 3601 caggatctct ctgccctgac tgggatacc ctgaaagtc tttctgctgt tgacactttg  
 3661 caagaggatg aggcctctct ggccaagaga aagcattcta ctgcaaaaa acttcccac  
 3721 agctggagca atgtcatctg tgcagagggt etaggcagca tggagatcgc tggagagaag  
 3781 aaataccagt attatagcat gccctcttct ttgtgagga gccctggctg aggccggcat  
 3841 ccccacagag tgcagagggg ggcactctt gagattaca acagtaaaag agaggctaca  
 3901 aatgtaagaa atgaccagga aaggcaagaa acacaaagta gtatagtggg tttctgggtg  
 3961 tctctaaaca ggcaagcaca ctcaaagtat ggccagtctc tttctgtccc ctctaacta  
 4021 aagcgagttc cttttcagc agaaactgtc ttgcctctgt ccagaccctc tgtgccagat  
 4081 gtgctggcaa ctgaacagga catccagact gaggttcttg ttcactgac tgggcagacc  
 4141 ccagtgtct ctgactgggc atcagtggat gaaccaagg aaaagcagca gccatttctg  
 4201 cacttactgg atggacaaga caaggcagag caagtgtctc ccacttgag ttgcacacct  
 4261 gaacccatga caatgagctc cctcttctcc caagccaaga tcattgcaaac tggaggtgga  
 4321 tatgtaaact gggcatttct agaaggtgat gaaactgggt tgtttagcat caagaaaaag  
 4381 tggcaaacct gcttgcctc caattgtgac agtgattctc ctggagtgca acagcaccag  
 4441 aagcagggcc aggcagctc cctatctgat aactcaaca gatcggccca gtagtgtaa  
 4501 tgctcagagg tgggaccatg gcttcagcca aacacactct tttgatcaa tctctccgc  
 4561 agatacaggc ccttcctag gagtcagtag tttagattcc ataaggagga gaaattgatg  
 4621 aagatctgta agattaaaaa tcttccagc tcttcagaaa tagggcaggg agcatgggtc  
 4681 aaagcagaaa tgctaacca agacaggaga ctgtcaaga aaaagaagaa tactcaagga  
 4741 ctccagggtc caatcataac agtcaatgcc tgcctcaga gtgaccagt gaatccagag  
 4801 ccaggagaaa acagcatctc tgaagaggag tacagcaaga actgggtcac agtgcctaaa  
 4861 ttagtcaca cagggttaga accttacata catcagaaaa tgaactaa agaaattgga  
 4921 caatgtgcta tacaatcag tgattacct aagcagctc aagaggatct cagcaaaaaac  
 4981 tcttttgga attccaggag caccaacctc aataggaaact cctgtctgaa aagtcaatt  
 5041 ggagttgaca agatctcagc cctctaaaa agcctcaag agcctacca tcattatca  
 5101 gccattgaaa ggaataattt aatgaggtt tctcagaca taccattac accagtccaa  
 5161 ctgtttgcag gagaagaaat aactgtctac aggttggagg agagtccccc tttaacctt  
 5221 gataaaagca tgcctcttg gtctcagct gggagagcgg caatgatcca ggtattgtcc  
 5281 cgagaggaga tggatggggg cctccgtaaa gctatgagag tctcagcac ttggtctgag  
 5341 gatgacattc tcaagccggg acaagtctt attgtcaagt ccttctctc tgaggttggtg  
 5401 cggacatgac ataaatctt ccaggagagc actgtgcttc atctttgct cagggaaatt  
 5461 caacaacaaa gagctgtca aaaattgac tatacctca accaagtga accacaaacc  
 5521 atacctaca caccaagggt cctggaagt ttcttaact actgcatc agccaaccag  
 5581 tgggtgacca ttgagaagta tatgacagg gagtccgga agtataaca caacaatggt  
 5641 gatgaaatca ccccaccaa caccctggag gagctgatgt tggcttctc tcaatggacc  
 5701 tatgagtaca ctgggggaga gctgtggtt ttgatttgc aaggtgttg agaaaattg  
 5761 acagatccat ctgttataaa acctgaagtc aaacaatca gaggaatggt tttggaccg  
 5821 gccatttgg gggaagatgc aattagaac ttcattgcaa aacatcattg taactctgc  
 5881 tgcgggaage tcaaacctcc ggatttaaaa agaatgact attccctga aaggataaat  
 5941 tccaccttg gacttgagat aaaaatagaa tcagctgagg agcctccagc aaggagacg  
 6001 ggtagaaatt cccagagaa tgatatgcaa ctataaaaag ggaggagcaa gaagatccca  
 6061 gtgcttgcct tgcctgccag gaactctgtg ataacataga ttgatcaacg tgatgtgat  
 6121 tacatcagcg tctcttggg acacgcttc tgaactcac atctctctt gtcaaaggc  
 6181 ctcatggta tatgatcaat gggcttctc agacactgac ctctgacag ggcacttgc  
 6241 agctccatcc tcaagtcca caggaagatg ctggatgag tcagctggga atattgtct  
 6301 tgtgactcct attgcttag ctggtcactt ggaacttgg agcagaatcc tgcattaa  
 6361 aggatgggtg tgggggggat acatttattt tatcttca ctatgtatgc agactggacc  
 6421 cctactact attgtcac tcaccacag attgtattta tctctatata tatgtcata

Figure 9A

6481 aaaagttatg tgatttecte ctegtctttt tccacaacat aggacttga atagcaatga  
 6541 taggaaaaac aatggaacaa ggggtgggtt gcacagattg gagcacatc ctgcacaaac  
 6601 tacciaagtat actgggtgaaa tctcgatggg ttccagatat tgcagtgaa tcatatgatg  
 6661 cctggatatt tcagggttct gtaaaagaaa gggaaaccta aaacaaatac ccttccatat  
 6721 ataataata tggaatatgt atattatata ttttttata tatataatat atatggaata  
 6781 tatatattat atataataaa tacatatgga atatatatat tttatatata tatatatatt  
 6841 tttatttttg agatggaggt tcactctttt taccagget ggagtgcatt gatgcgatct  
 6901 cactgcaacc tctgcctccc gggttgagc gattcttggt tctcagttct cgggtagct  
 6961 gggactacag gtgtgcacca ctatgctgg ctaatttgg atttttagta gagatggggt  
 7021 ttcacatgt tggccagggt ggtctcaaac tctgacctc agatgatcca cctgccttgg  
 7081 ctcccaaaag tctggggtt acaggcgtga gccactgcgc ctggcctttt tttttttt  
 7141 tttaaacgag aacaagaata tgaagaactg gaaatcatta agaaagggtt tcccttctt  
 7201 aaagctcagg ggtactatta gttaggaggt gactaactca acctgtaaaa caccactct  
 7261 ccttccaaag ttgtatatat aatattgcag gttaaattac tttatgtcag gtcctatgaa  
 7321 gaaagatacg gtttcagact gaaaacatgt ttcacagggtg ttgtcttct tccagagcag  
 7381 agttccctat tccctggca taaagaatgt atatatatt tgaaatatgg ctgagaacat  
 7441 gtcattgggt tgtgaggcct aaggtaage actcctggca gccacactgt gtagtgatt  
 7501 tgagggatca gtcacccctc ttgtatgtg ggcttggtg ccttacctcg aacaagcacc  
 7561 agctttcac acaaggagag atgtggggtt gggagtcctc tcccatctct attgcctc  
 7621 cttcttatt ataagctgt ccagttcaca ggcagcaaac ctctgggtt tgaaaaattc  
 7681 caacttatt ttatctttaa tctgacatt agctgacttg ctagtgcct tcttataaa  
 7741 atctacactc ttgcattctt aggcatacag gggaaatgt gaaaaggaag gtggaaaacc  
 7801 aagaatttag ttgccaatg attgctctg attctttaa gtttgagttc cacaagggt  
 7861 aatttatcc cctttactt ggggtttggg gtggtggaaa gcgggaaatt tgggtgatt  
 7921 gttgattggc aatgaggata aaatgtaat actttttgg ggacttaaca actttatct  
 7981 attetacaag tcagtaaagg aacaattggt actcacctca gtgtgcact caactatgga  
 8041 aagaggcaga gtttcttgc ccaattgcca aactaaagac atcagttcat tggtaata  
 8101 ttgttacct ggaatggaac ttgaaagcaa atacatttgg atttcaaatt tcaaaaaa

Figure 9A

MSQKSWIKGVFDKRECSTIIPSSKNPHRCTPVCQVCQNLIRCYCGRLIGDHAGIDYS  
 WTISAAGKESEQWSVEKHTTKSPTDTFTGTINFQDGEHTTHAKYIRTSYDTKLDHL  
 LHLMLKEWKMEPKLVISVHGGIQNFTMPSKFKEIFSQGLVKA AETTGAWIITEGI  
 NTVSKHVGDAKSHSSHSLRKIWTVGIPPWGVNIENQRDLIGKDVVCLYQTLDNPLS  
 KLTTLSNMHSHFILSDDGTGKYGNEMKLRRNLEKYLSQLKIHCRSRQGVVVG  
 VVEGGPNVILSVWETVKDKDPVVVCEGTGRAADLLAFTHKHLADEGMLRPQVKE  
 EIICMIQNTFNFSLKQSKHLFQILMECMVHRDCITIFDADSEEQQDLDLAILTALLK  
 GTNLSASEQLNLAMAWDRVDIAKKHILIYEQHWKPDALQAMSDALVMDRVDFV  
 KLLIEYGVNLHRFLTIPRLEELYNTKQGPTNTLLHHLVQDVKQHTLLSGYRITLIDI  
 GLVVEYLIGRAYRSNYTRKHFRALYNNLYRKYKHQRHSSGNRNESAESTLHSQFIR  
 TAQPYKFKEKSIVLHKSRRKSKEQNVSDDPESTGFLYPYNDLLVWAVLMKRQKMA  
 MFFWQHGE EATVKA VIACILYRAMAHEAKESHMVDDASEELKNYSKQFGQLALD  
 LLEKAFKQNERMAMTLLTYELRNWSNSTCLKLAVSGGLRPFVSHCTCTQMLLTDM  
 WMGRLKMRKNSWLKIIHILPPTILTLEFKSKAEMSHVPQSQDFQFMWYYSQNA  
 SSSKESASVKEYDLERGHDEKLDENQHFGLESQHQLPWTRKVYEFYSAPIVKFW  
 FYTMAYLAFLMLFTYTVLVEMQPQPSVQEWLVSIYIFTNAIEVVREVSISEPGKFTQ  
 KVKVWISEYWNLTETVAIGLFSAGFVLRWGDPPFHTAGRLIYCIDHFWFSRLLDFF  
 AVNQHAGPYVTMIAMTANMFYIYIIMAVLLSFGVARKAILSPKEPPSWSLARDIV  
 FEPYWMIYGEVYAGEIDVCSQSPCPPGSFLTPTFLQAVYLFVQYIIMVNLLIAFFNNV  
 YLDMESISNNLWKYNRYRYIMTYHEKPWLPPPLILLSHVGLLLRRLCCHRAPHDQ  
 EEGDVGLKLYLSKEDLKKLHDFEEQCVEKYFHEKMEDVNCSCERIRVTSERVE  
 MYFQLKEMNEKVSFIKDSLLSLDSQVGHQLQDLSALTVDTLKVL SAVDTLQED EALL  
 AKRKHSTCKKLPHSWSNVICA EVLGSMEIAGEKKYQYYSMPSSLLRSLAGGRHPP  
 RVQRGALLEITNSKREATNVRNDQERQETQSSIVVSGVSPNRQAHSKYGQFLLVPS  
 NLKRVPFSAETVLP LSRPSVPDVLATEQDIQTEVLVHLTGQTPVVS DWASVDEPKE  
 KHEPIAHL LDGQDKAEQVLP LTLCTPEPMTMSSPLSQAKIMQTGGGYVNWAFSEG  
 DETGVFSIKKKWQTCLPSTCSDSSRSEQHQKQAQDSSLSDNSTRSAQSSECSEVGP  
 WLQPNTSFWINPLRRYRPFARSHSFRFHKEEKLKMKICKIKNLSGSSEIGQGA WKA  
 KMLTKDRRLSKKKKNTQGLQVPIITVNACSQSDQLNPEPGENSISEEEYSKNWFTV  
 SKFSHTGVEPYIHQKMKTK EIGQCAIQISDYLKQSQEDLSKNLWNSRSTNLNRNSL  
 LKSSIGVDKISASLKSPQEPHHYS AIERNLMLRLSQTIPFTPVQLFAGEEITVYRLE  
 ESSPLNLDKSMSSWSQRGRAAMIQVLSREEMDGGRLKAMRVVSTWSEDDILKPGQ  
 VFIVKSFLPEVVRTWHKIFQESTVLHLCLREIQQQRAAQKLIYTFNQVKPQTIPYTP  
 RFLEVFLIYCHSANQWLTIEKYMTGEFRKYNNNNGDEITPTNTLEELMLAFSHWY  
 EYTRGELLVLDLQGVGENLTDP SVIKPEVKQSRGMVFGPANLGEDAIRNFI AKHHC  
 NSCCRKLKLPDLKRNDYSPERINSTFGLEIKIESAEPPARETGRNSPEDDMQL

Figure 9B

**Figure 10A**

**Figure 10A**

FOOTPRINT 26222360

601-1-098CIP

MEVAWL VVVLGQQPLARQEGQSRLVPGRLVLWPLGRSSWPVAVDLAPARPRGPLICHTGHEQA GREPG  
 PGSSTKGPVLHDQDTRCAFLPRPPPLQTRRYCRHQGRQSGGLGAGPGAGTWPAPPGVSKPRCPGRARPGEQQQ  
 VTTARPPAINRGARQPRAGAAAAGRPGAGAWRTGEAAAASAGPAVGEAGGAMGSRRAPTRGWGAGGRSGAGGDGE  
 DDGPVWPSPASRSYLLSVRPETSSNRLSHPSSSRSTFCSSIAQLTEETQPLFETTLKRSVSESDVRFTCIVTGYPEP  
 EVTWYKDDTELDRYCGLPKYEITHQGNRHTLQLYRCREDAAIYQASQNSKGVSCGVLEVGTMTYKIHQRWF  
 AKLKRKAAAALREIEQSWKHEKAVPGEVDTLRLKLSDFRQRRRLSGAQAPGPSVPTREPEGGTLAAWQEGEGETETA  
 QHSGGLINSFASGEVTTNGEAAAPENGEDGEHGLLTYICDAMELGPQRALKEESGAKKKKKDEESKQGLRKPELEKA  
 AQRRRSSENCIPSSDEPDCGTQGPVGEVQVQTQPRGRAARPGSSGTDSTRKPASAVGTPDKAKAPGPGQEVYF  
 SLKDMYLENTQAVRPLGEEGPQLSVRAPGESPKGAPLRARSEGVPGAPGQPTHSLTPQTRPFNRKRFAPPKPKG  
 EATTDSPISLSQAPECCGAQSLGKAPPQASVQVPTPPARRRHGTRDSTLQQAAGHRTPEVLECCQTTTAPTMSASSS  
 DVASIGVSTSGSQGHIEPMDMETQEDGRTSANQRTGSKKNVQADGKIQVDRTRGDGTQTAQRTRADRTQVVDAGT  
 QESKRPQSDRSQAQKGMMTQGRAETQLETTQAGEKIQEDRKAQADKGTQEDRRMQGEKMQGEKGTQSEGSAPTA  
 MEGQSEQEVATSLGPPSRTPLPPTAGPRAPLNEICFVQTPGSCFPKPGCLPRSEAAVVTASRNHEQTVLGPLSGNL  
 MLP AQPPHEGSVEQVGGERCGRGPQSSGPVEAKQEDSPFCPEERPGGVPCMDQGGCPLAGLSQEVPTMPSLPGTG  
 LTASPKAGPCSTPTSQHGSTATFLPSEDQVLMSSAPTLHLGLTPTQSHPETMATSEGACAAQVPDVEGRTPGPRSC  
 DPGLIDSLKNYLLLLKLSSTETSGAGGESQVGAATGLVPSATLPTVEVAGLSPTSRRILERVENNHLVQSAQTL  
 LSPCTSRRLTGLLDREVQAGRQALAAARGSWGPGPSSLTPVAIVVDEEDPGLASEGASEGEVLEGPGLLGASQES  
 SMAGRLGEAGGAAPGQPSAESIAQEPSQEEKFPGEALTGLPAATPEELALGARRKRFLPKVRAAGDGEATTPEER  
 ESPTVSPRGRKSLVPGSPGTPGRERRSPTQGRKASMLEVPRAEEELAAAGDLGPSKAGGLDTEVALDEGKETLAKP  
 RKAKDLKAPQVIRKIRVEQFPDASGSLKLWCQFFNILSDSVLTWAKDQRPVGEVGRSAGDEGPAALAIQASPVDC  
 GVYRCTIHNEHGSASTDFCLSPEVLSGFISREEGEVGEIEIEMTPMVFAGLADSGCWGDKLFGRLVSEELRGGGYGC  
 GLRKASQAKVIYGLEPIFESGRTCHIKVSSLLVFGPSSSETSLVGRNYDVTIQCKIQNNMSREYCKIFAAEARAAPGFGEV  
 PEIPLYLIRPANNIPYATLEEDLGKPLESYCSREWGCAEAPTASGSSEAMQKCCQTFQHWLYQWNTNGSFLVTDLAGV  
 DWKMTDVQIATKLRGYQGLKESCFPALLDRFASHQCNAVCELLGLTPLKGPEAAHPQAKAKGSKSPSAGRKGSQ  
 SPQPKKGLPSQGTGRKSPSSKATPQASEPVTTLQGGPPTQEEGSKAQGM

Figure 10B



T03727 2622860

ATGAATAATCAAAAAGTGCTAGCTGTGCTACTGCAAGAGTGCACAAAGCAAGTGCTGGATCAGCTCTTGTTGGAAAGCGCCAGATGTGTGGAAGAGGACAA  
GAGGAGGACCAAGCGCTGACAGAGCTTTACTCCCCAGCGAGTTAAGGACCCCTGATCCAGGAGGCAAAAGGAAATGAAGTGGCCCTTCGTGCTGAAAAAGT  
GGCAGTACAAACAAAGCGTGGCCAGAGGACAAACAACTGAAGGATGTGATGGCGCCGGTTCAGCAGCTTACGAGCTTACGGCTTCGAGGGCTGCC  
ATCCCTGCTCGGACTGTGGCGTGGCGGCTATGTTGTTCTGGTGAACGGTTCCTGTATGGCTCAGCGTCTCTGGAACAACTTTTAAAGCA  
AAAGGCTCCACAAGTTGCAGCCAGCCACGCAATGGAGCAACGGGTACTGGCTGTACAGAAATGAAAGTGACAAAGTCTCGTGCAGTCCGCTCAGCCG  
GAGTATATCTGAGCAGTCTAATAGCAACAATGGAGCAACGGGTACTGGCTGTACAGAAATGAAAGTGAAGTGAATATTTGGCACTTCTCAGCCG  
CAGATCAGAGGGCAGATTCTCAAAAAGCTGGGTATGTGTCACGACAGATTAATAATGGCCCTCCATGACCAAGAAAGATTAAGAAAGTTTAAACAAATCCACAATTA  
GATAAAAGGCTCTCCACGTCGTAGGTATCTGGCAGACATCTTTGTTCCATGCAAGCAAGAGCTGCCCTCAGTGCCTATACGCCGCTCTCTCGTGC  
ATTTGAGCCTGCTGAAGGATTTGACCAATTTGCTGCTCGCTGACAGAACCTTCAGAAATGAAAGTGTCTCCAGAAATGAAAGTGTCAAGCTTTCGCTTCCAGCT  
TCACAGCTGTGAATATCCGTGGCACCTGTATTATGTCTACAGTATGAGCTTCAAGCTTCACAGCTTCACAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCT  
GGCCTTTGAGATTGGCTCTCACCAAGAGAGATGATGAGCTGTACTGGAAACAGGAGCTTCAGAAAGCAATTTGGAAGCTTCAAGCTTCAAGCTTCAAGCT  
AGTGCACAGAAAGCTCCATGGGAGACAGGACCGTCCATGACAGCAAGTCACTGTGTAGGAAAGCAATTTGGAAGCTTCAAGCTTCAAGCTTCAAGCT  
CCAGAAGTCAAGACAGAGAGCTCTGTCTCAAGAAATTAATGTCTGTATGGCCAGGTGAAGGAAATTTCAAGCTTCAAGCTTCAAGCTTCAAGCT  
ACAGATCTTATGTTCCGAGAGTATTGAAGTATTGTGGAAACAAACAAATGAACAGAAAGTGCACAAACAGGAGTCTGATCACTGCTTCAAGCTTCAAGCT  
CCATACTCGTGTGAGTATTGAAGTACTACTCAAGAAAGGCAATTTGATGCTCTCTGGATCAAGATGTGGAAGCTGAGACTGAGCCATCGG  
AGAAATAAAACATAGATACTGTGAGTACTACTCAAGAAAGGCAATTTGATGCTCTCTGGATCAAGATGTGGAAGCTGAGACTGAGCCATCGG  
GAGGAACTCAGAAAGGAGGAGGAGTGTTCACAAAGTCTGAGTGGCAGCCAGACTTCCAGTGTGGAGCAACTTCAAGGTTTAGTTCACCTGCTGTCTG  
ACTACAGCAATGGTGAAGGAGTGTTCACAAAGTTCAGACAGGTCAGCCAGAAAGAGCGCTGGCAAGAAACATCTGTTCAAGAAACCAACATGACAATTTGGAGC  
GCTGGAGGAACTGAATTAATCAGTTGACAGGGAAGGAGAGCTATGCAATTCATTGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCT  
AGGAGCTAGAGATGACAGGGAAGGAGAGCTATGCAACCTTCTCGCTCATAATACCCAGGCAATTTCTGGCCCTGTTGAGCTTCAAGCTTCAAGCT  
CTTCTCAAAATCAGCCACAGCAACAGATGCCCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCT  
AGCTCCAGAAAGTATCCAGGAAGTCAAGAAATATGGACCCAGAAATATTTGAGTTCAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCT  
GGTAGGCCCAAGAAATAGGGCACACATCCCTTCAGTCCAAAGAAAGAGGCTTGAATAATTTGAGTTCAGCTTCAAGCTTCAAGCTTCAAGCT  
AGGAGGGGAAAGAGCAGGGAGAAATAGTGAAGAGGGGAGGCTTCAATTTCTGGGAAACATTTCCATGCTGCTCCATGAGTTCCTTCAAGCTTCAAGCT  
AGAAAGCACTGAAGATGCAACCTTAGCTTACAGGGTCTGCAATTTCTGGGAAACATTTCCATGCTGCTCCATGAGTTCCTTCAAGCTTCAAGCT  
CCTGTTCAAAATCCTGACTCCAGAAAGTGGTGGCCAGTCCAGAGAGGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCT  
CGACAGCTGGATGTTCCCTGCAACAAATGGGCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCT  
TGTAAGCGGTAACTCCTTCCCTGCTCAGCGGAGGCTGCAATTTCCAGTTCATCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCT  
CAGCTCATCTCAGTGTGGTGAATCAGCTGCAATTTCCAGTTCATCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCT  
TTGGGTTTCAATGGCCGGAAGATGAGGAAAGATCTTTAGCCAGTCAATCCACCGAGCAGATAGTCTTTTGTAAATATTTCAAAATAATCTGAA  
TTGGCTTTTTCAGAGACTAGAGAAATACGGGGTATTAAGCCAGTCAATCCACCGAGCAGATAGTCTTTTGTAAATATTTCAAAATAATCTGAA  
CTGTGAAGGAAATTTCCAGAGAAATATTTGAGGAGTATTAAGCCAGTCAATCCACCGAGCAGATAGTCTTTTGTAAATATTTCAAAATAATCTGAA  
CAAGAGAAATTTCCAGAGAAATATTTGAGGAGTATTAAGCCAGTCAATCCACCGAGCAGATAGTCTTTTGTAAATATTTCAAAATAATCTGAA  
GCACTATGTGACAGAAATTTCAAGAGAAATATTTGAGGAGTATTAAGCCAGTCAATCCACCGAGCAGATAGTCTTTTGTAAATATTTCAAAATAATCTGAA  
ACAAATAGGAGGATGATCAGTGTGGAGCCTTACATATTTGAGGAGTATTAAGCCAGTCAATCCACCGAGCAGATAGTCTTTTGTAAATATTTCAAAATAATCTGAA  
GAATATGGCTGGCTATGGCAATTTTCTATGATTTCTAATCATAGAGATTTGAGGAGTATTAAGCCAGTCAATCCACCGAGCAGATAGTCTTTTGTAAATATTTCAAAATAATCTGAA  
TCATCTACCTCAGAGATCCCGATTCATCCGTTGATCAGAAAGTTTCACTACCAATTTTGGAAAGAGAGGAAATTTTACTTCTTTAATAACCCAGCAT  
GTGGAATGTAATGAAATCTGGCATCGTCTTTTGACTAGACCTTCAATGGAGAAACCA

Figure 11A



FOI b7E b7C b7D

MNNQVAVLLQECKQVLDQQLLEAPDVSEEDKSEDQRCRALLPSELRTLIQEA KEMKWPFFVPEK  
WQYKQAVGPEDKTNLKDVGAGLQQLLASLRASILARDCAAAAIVFLVDRFLYGLDVSGKLLQVA  
KGLHKLQATPIAPQVVIRQARISVNSGKLLKAEYILSSLISNNGATGTWLYRNE SDKVLVQSVCIQI  
RGQILQKLG MWYEA AELIWA SIVGYLALPQDPDKGLSTSLGILADIFVMSKNDYEKFKNNPQINLS  
LLKEFDHLLSAAEACKLAAAFSAVTPLFVLTA VNIRGTCLLSYSSND CPPELKNLHLCEAKEAFEI  
GLLTKRDDPEVTGKQELHSFVKA AFGLT TVHRR LHGETGTVHAASQLCKEAMGKLYNFSTSSRSQ  
DREALSQEVM SVIAQVKEHLQVQSFSNVDDRSYVPESFE CRDLKLHGGQDFQKILDYTSQHHTSV  
CEVFESDCGNNKNEQKDAKTGVCITALKTEIKNIDTVSTTQEKPHCQRTGISSSLMGKNVQRELRR  
GGRRN WTHSDAFRVS LDQD VETETEPSDYSNGE GAVFNKSLSGSQTSSA WSNLSGFS SSWEEVNY  
HVDDRSARKEPGKEHLVDTQCSTALSEELENDREGRAMHSLHSQ LHDLSLQEPNNDNLEPSQNQPQ  
QQMPLTPFSPHNTPGIFLAPGAGLLEGAPEGIQEV RNMGPRNTSAHSRPSYRSASWSSDSGRPKNMG  
THPSVQKEEAFEIIVEFPETNCDVKDRQGKEQGE EISERGAGPTFKASPSWVDPEGETAESTEDAPLD  
FHRV LHNSLGNISMLPCSSFTPNWPVQNPDSRKSGGPVAEQ GIDPDASTVDEEGQLLD SMDVPCTNG  
HGSHRLCILRQPPGQRAETPNSSVSGNILFPVLSEDC TTTTEEGNQPGNMLNCSQNSSSSVWWLKSP  
AFSSGSSEGDSPW SYLNSGSSWVSLPGKMRKEILEARTLQPD DFEKLLAGVRHDWLFQRL ENTGV  
FKPSQLHRAHSALLKYSKKSELWTAQETIVYLG DYLT VKKKGRQRNAFWVHHLHQEEILGRYVVG  
KDYKEQKGLWHHFTDVERQMTAQHYVTFENKRLYEQNIPTQIFYIPSTILLILEDKTIKGCISVEPYI  
LGEFVKLSNNTKVVKTEYKATEYGLAYGHFSYEF SNHRDVVVDLQGWVTGNGKGGLIYLTDPQIHSV  
DQKVFTTNFGKRGIFYFFNNQHV ECNEICHRLSLTRPSMEKP

Figure 11B

A

HeEF-2\_kinase>  
 MHCK\_B>  
 Melanoma\_kinase>  
 Kidney\_kinase>  
 Muscle\_kinase>  
 Heart\_kinase>  
 Lymphocyte\_kinase>  
 consensus

1 ALDD--EILKKAQSPFGG--  
 1 ACT--ATLKAQEPVFAES--  
 1 QOLGCAKEFLSKBEMGG--  
 1 FQGRGAAMQKLSBEMDG--  
 1 GDK---FGRVSVSELKRG--  
 1 EGR---FQGAFAELHFG--  
 1 EAQETLYVGDYLVKKK--  
 1 wt v i m s e g

HeEF-2\_kinase>  
 MHCK\_B>  
 Melanoma\_kinase>  
 Kidney\_kinase>  
 Muscle\_kinase>  
 Heart\_kinase>  
 Lymphocyte\_kinase>  
 consensus

62 PRHMEALGGEENRHKPKQ--  
 56 KQAMIAKADKNSPKPK--  
 74 QOQRAQALTFARQMKSI--  
 74 QOQRAQALTYENOVKEOTI--  
 75 CKQMSRECKIPAAEAAPGFG--  
 73 CYQNTATYAKIVAAEAQPLEGFG--  
 58 FERGNTQVTEFKRLYEONIPQ--  
 81 v lQ akkw fn kp

HeEF-2\_kinase>  
 MHCK\_B>  
 Melanoma\_kinase>  
 Kidney\_kinase>  
 Muscle\_kinase>  
 Heart\_kinase>  
 Lymphocyte\_kinase>  
 consensus

130 LTPOAFSHITERRGHQIMVQ--  
 124 NTPQFSSHITERRGHQIMVQ--  
 145 EIMLAFSHITERRGHQIMVQ--  
 145 EIMLAFSHITERRGHQIMVQ--  
 154 QKCTFOHVVCKISSCLLVQ--  
 150 QKCTFOHVVCKISSCLLVQ--  
 132 EYGLAFSHITERRGHQIMVQ--  
 161 afshwtyeyt g llvvdllg vg

HeEF-2\_kinase>  
 MHCK\_B>  
 Melanoma\_kinase>  
 Kidney\_kinase>  
 Muscle\_kinase>  
 Heart\_kinase>  
 Lymphocyte\_kinase>  
 consensus

196 ESMGAPF  
 190 QYENQSF  
 216 EKLKIPDR  
 216 EKLKIPDR  
 221 ELLGTPQ  
 217 EMLGKSY  
 206 ERLSSTRP  
 241 r l l i

Figure 12

TOPP "26236960

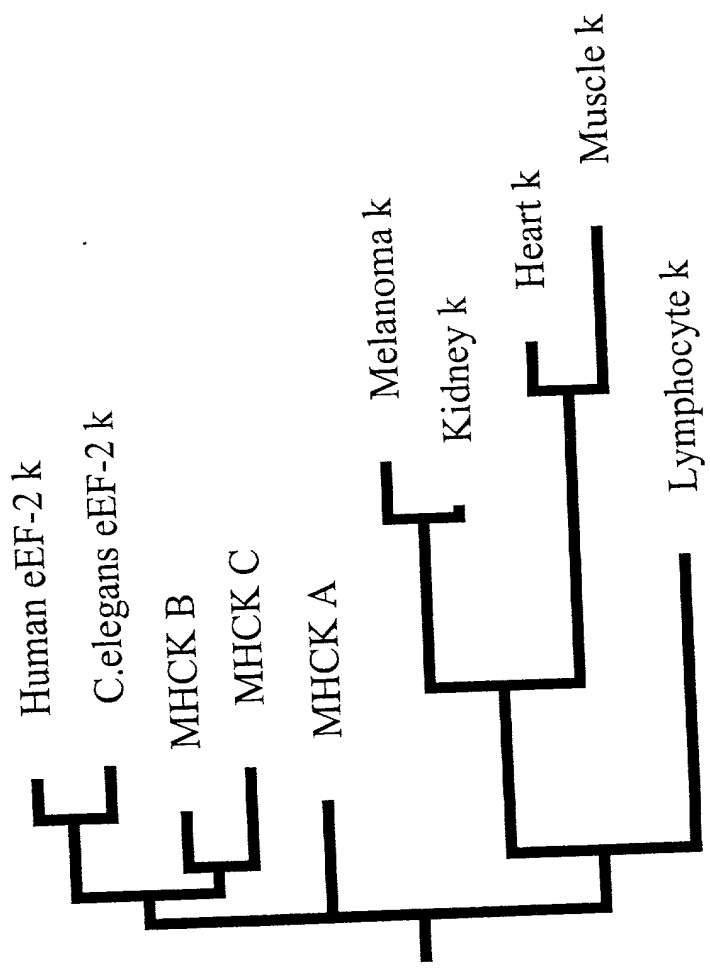


Fig. 1

Figure 13

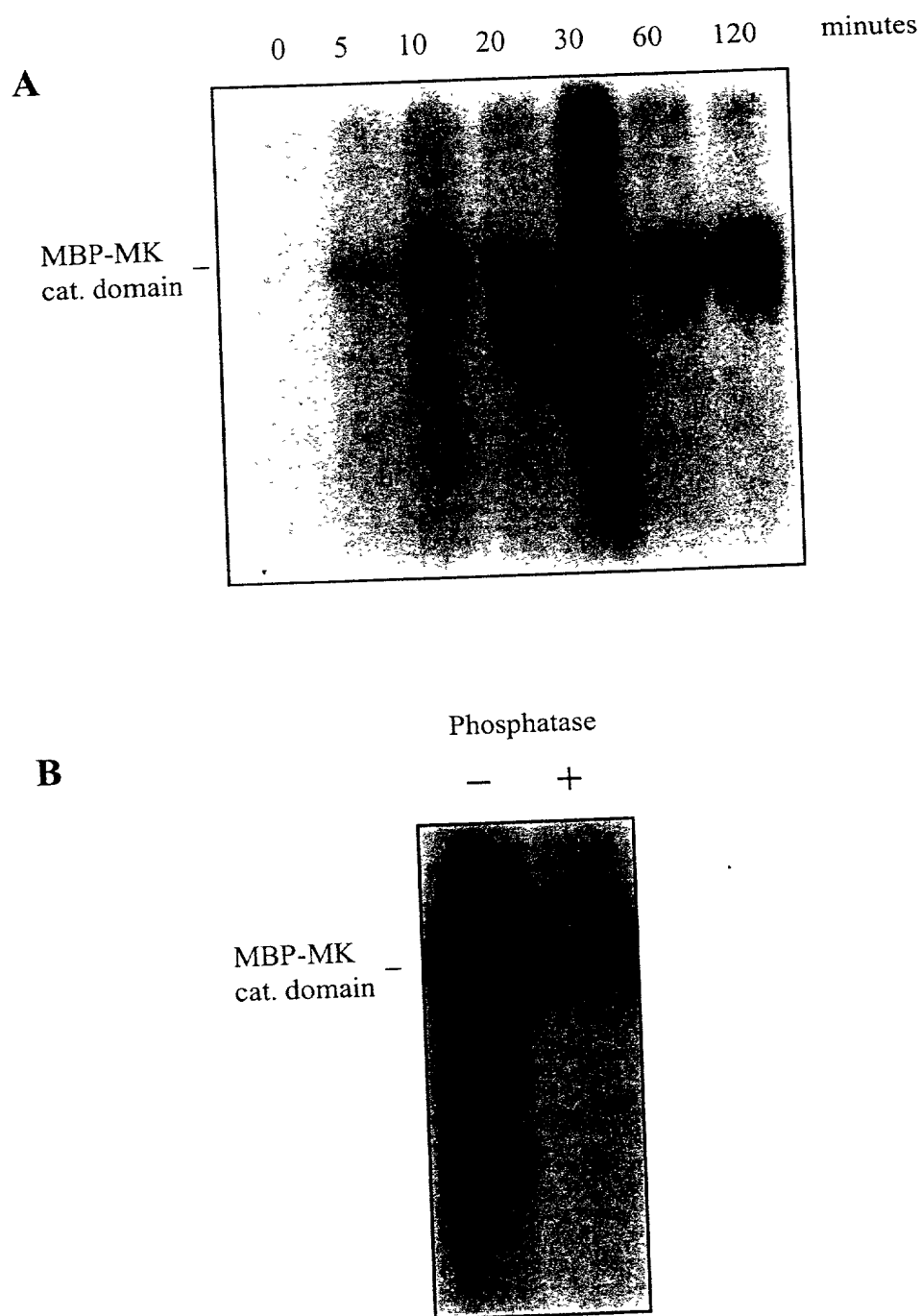


Figure 14

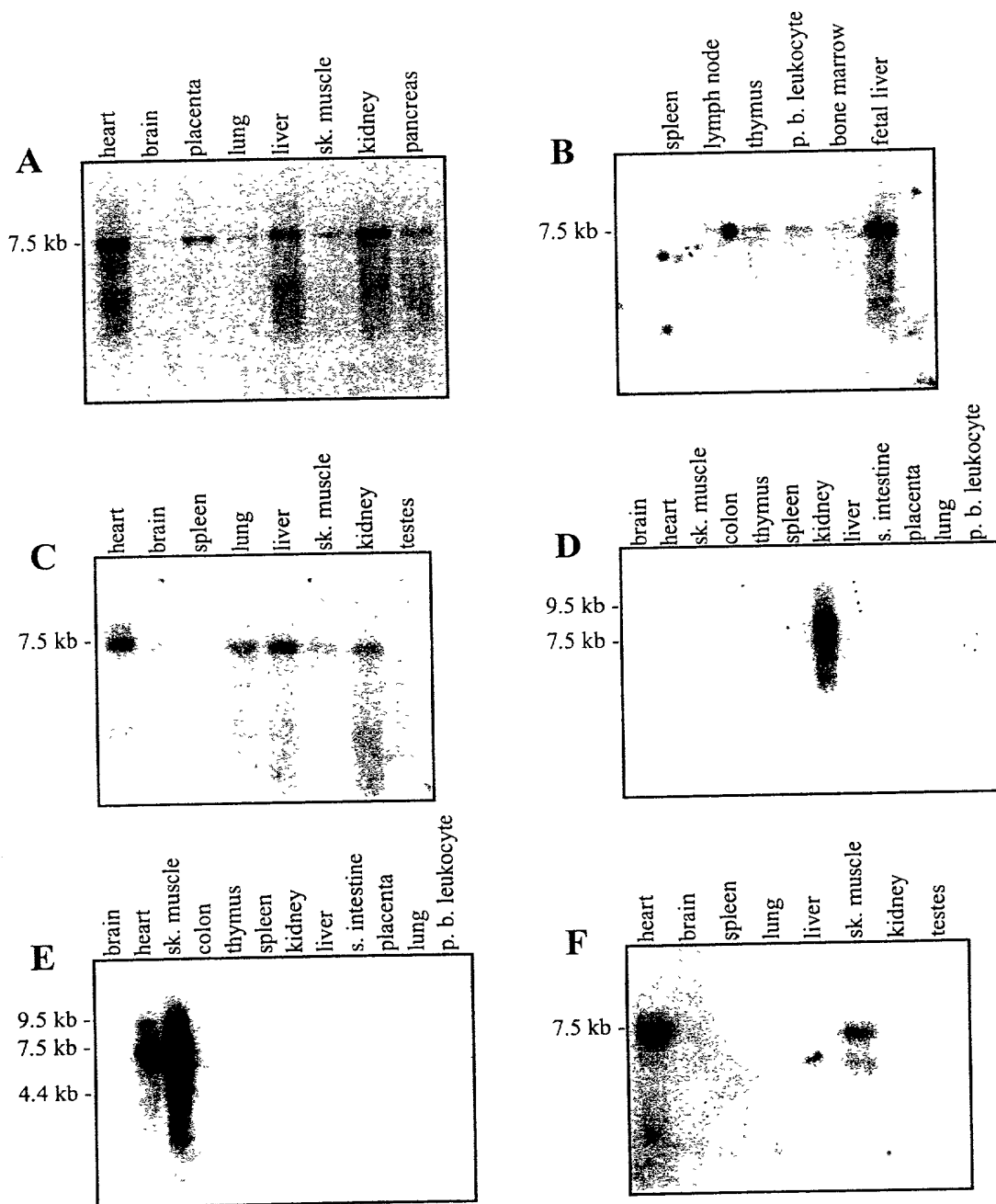


Figure 15

MK> 1 MSQKSWIESTLQKREYVIFSSKPHRCLPGCOICOOI QYGLKCHOCPTA LA  
 KK> 1 MSQKSWIESTLQKREYVIFSSKPHRCLPGCOICOOI QYGLKCHOCPTA LA  
 ME> 1  
 MK> 61 KYSDVILQDHPNCAIEMSVKHEHCOSPTLA VINFCSSS KAKI KUTSVW  
 KK> 61 SAAKGE-----S-CHSVKHEHCOSPTLA VINFCSSS KAKI KUTSVW  
 ME> 1  
 MK> 121 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 121 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 15  
 MK> 181 ANHVGDAIMSSSERRKICTIGTAFHGVIELNOLVC DVAVYOTULPLSKM  
 KK> 181 ANHVGDAIMSSSERRKICTIGTAFHGVIELNOLVC DVAVYOTULPLSKM  
 ME> 75  
 MK> 241 NISHFILDEGTGVKYGABV LRPBUEH KCHOCPTA VINFCSSS KAKI KUTSVW  
 KK> 241 NISHFILDEGTGVKYGABV LRPBUEH KCHOCPTA VINFCSSS KAKI KUTSVW  
 ME> 135  
 MK> 301 MEYLOHPT PVVCEGTGAADLLA LKCHOCPTA VINFCSSS KAKI KUTSVW  
 KK> 301 MEYLOHPT PVVCEGTGAADLLA LKCHOCPTA VINFCSSS KAKI KUTSVW  
 ME> 195  
 MK> 361 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 361 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 255  
 MK> 421 DIANM EVVGCGLVGC-----  
 KK> 421 DIANM EVVGCGLVGC-----  
 ME> 315  
 MK> 438 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 438 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 375  
 MK> 483 SPYHPT LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 483 SPYHPT LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 435  
 MK> 543 NNRRSGRNTSSSTOLVSEEFNPAKCHOCPTA VINFCSSS KAKI KUTSVW  
 KK> 543 NNRRSGRNTSSSTOLVSEEFNPAKCHOCPTA VINFCSSS KAKI KUTSVW  
 ME> 494  
 MK> 601 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 601 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 583  
 MK> 663 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 663 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 539  
 MK> 723 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 723 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 699  
 MK> 783 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 783 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 703  
 MK> 843 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 843 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 819  
 MK> 903 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 903 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 808  
 MK> 963 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 963 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 959  
 MK> 1023 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1023 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 990  
 MK> 1070 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1070 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 979  
 MK> 1130 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1130 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1039  
 MK> 1184 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1184 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1099  
 MK> 1244 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1244 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1159  
 MK> 1259 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1259 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1174  
 MK> 1291 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1291 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1192  
 MK> 1337 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1337 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1210  
 MK> 1387 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1387 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1240

MK> 1434 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1510 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1270  
 MK> 1466 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1570 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1283  
 MK> 1503 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1630 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1310  
 MK> 1544 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1690 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1316  
 MK> 1603 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1750 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1370  
 MK> 1663 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1810 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1413  
 MK> 1723 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1870 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1462  
 MK> 1783 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1930 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME> 1515  
 MK> 1843 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 KK> 1990 LKLEWOMELPKLVISVHGC MFELFCGLKGLIKAT TGAH KCHOCPTA LA  
 ME>

Figure 16

Table 1. (continued)	
Variable	Value
Number of subjects	100
Age (years)	65.0
Sex (male/female)	50/50
Height (cm)	170.0
Weight (kg)	75.0
Body mass index (kg/m <sup>2</sup> )	25.0
Education (years)	12.0
Occupation	Professional
Marital status	Married
Smoking status	Non-smoker
Alcohol consumption	None
Exercise frequency	None
Family history of disease	None
Current medications	None
Comorbidities	None
Study duration	12 months
Follow-up period	12 months
Dropouts	0
Lost to follow-up	0
Completed study	100
Adherence to protocol	100%
Consent rate	100%
Approval by ethics committee	Yes
Registration number	123456789
Version	1.0
Date of publication	2023-10-27

### Figure 17A

```

MELANOMA_KINASE> 1837 QDEPSDENLQPGNSTEESTNSVRML-
KIDNEY_KINASE> 1963 FGLEIKIESAEEPPAFNGRNSPEDDQQL

```

### Figure 17B



601-1-098CIP

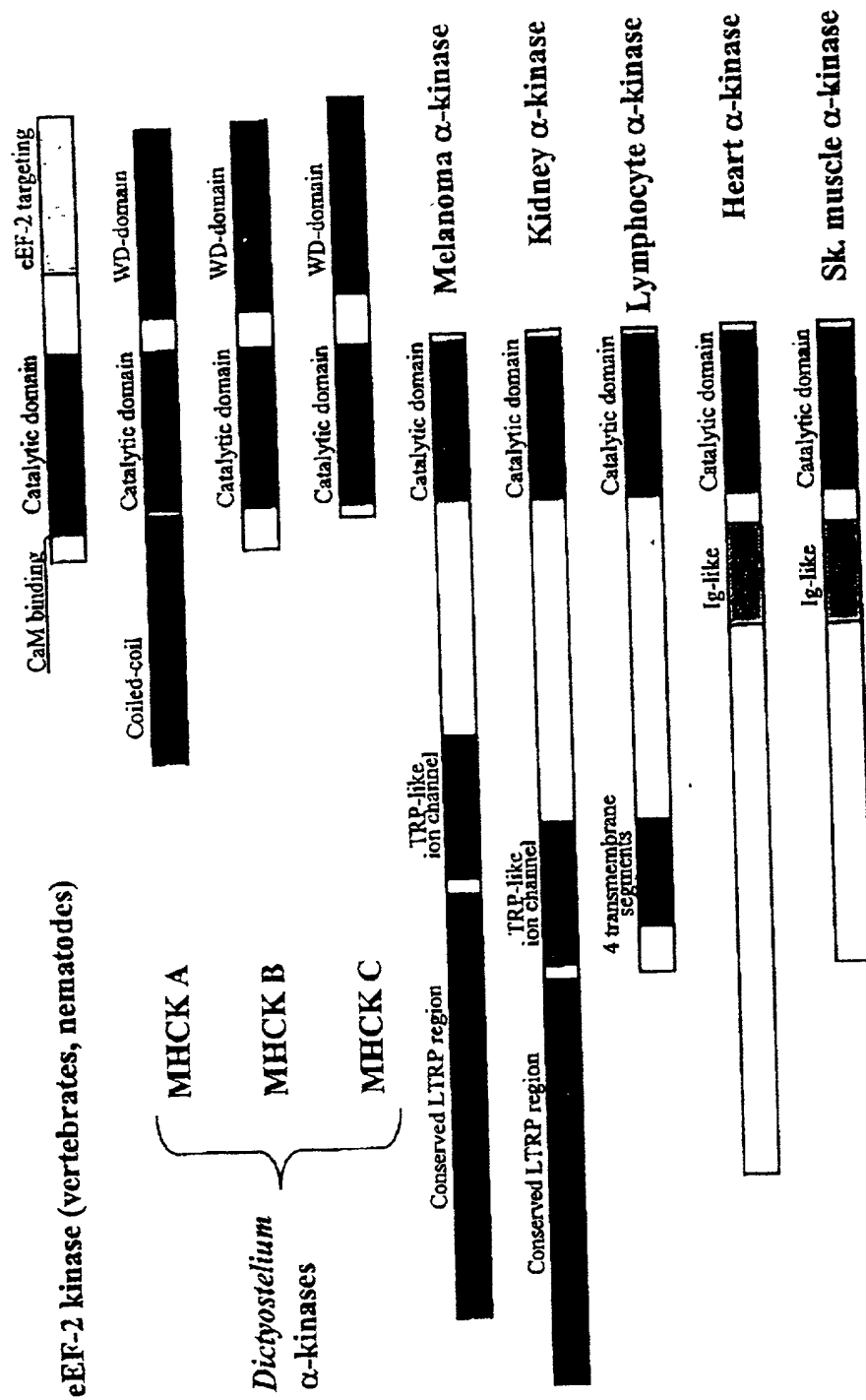


Figure 18

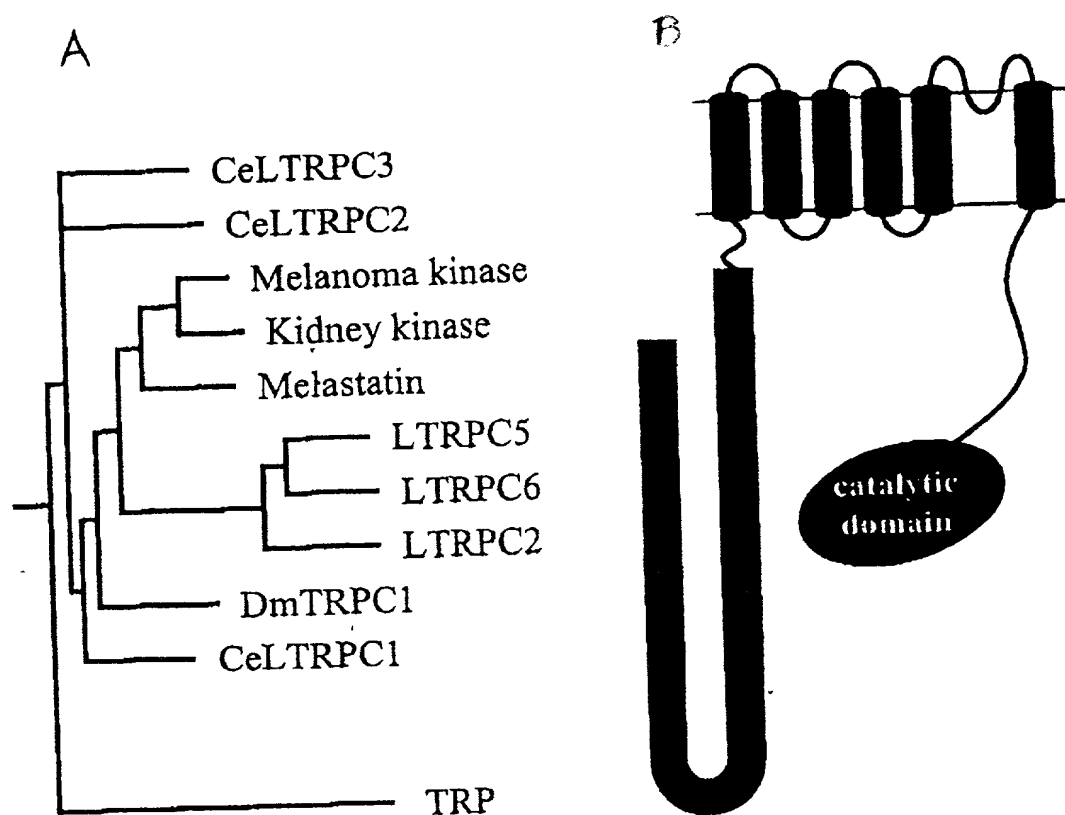


Figure 19